-153-

WE CLAIM:

1. A compound of Formula I:

where:

5

R¹ is hydrogen, halo, or C₁-C₄ alkyl;

m is 0, 1, 2, 3, or 4;

R is -(CH₂)_n-, -CH(CH₃)-, -C(CH₃)₂-, -CH₂-Q¹-CH₂-, or

-CH(OH)-CH(OH)-CH₂-;

Q¹ is CH(OH) or carbonyl;

10 n is 0, 1, 2, 3, or 4;

W-X-Y is -CH₂-CH₂-, -CH(R³)-N(R²)-CH(R³)-, -N(R⁴)-C(O)-CH₂-,

-C(O)-Q²-CH₂-, -CH(R^{3'})-O-CH₂-, or -CH(R^{3'})-N(R⁴)-C(O)-;

 Q^2 is $-N(R^4)$ - or $-CH_2$ -;

R² is hydrogen, -(C₁-C₄ alkylene)-R⁵, C₅-C₇ cycloalkyl, tetrahydropyran-4-yl, pyridinyl, pyrimidinyl, triazolyl optionally substituted with amino, benzothiazol-2-yl, 15 -C(S)-(morpholin-4-yl or C₁-C₄ alkoxy), -C(NR¹⁶)R¹⁷, -C(O)R⁶, -CO₂R⁷, -CO(NR⁸R⁹), -SO₂(NR⁸R⁹), -SO₂(C₁-C₄ alkyl), or an amino acid residue;

R³ and R^{3'} are independently selected from the group consisting of hydrogen and C₁-C₄ alkyl provided that only one of R³ and R³ may be C₁-C₄ alkyl;

R⁴ is hydrogen or C₁-C₄ alkyl: 20

> R⁵ is hydrogen, pentahaloethyl or trihalomethyl, cyano, hydroxy, C₁-C₄ alkoxy optionally substituted with C1-C4 alkoxy, C3-C6 cycloalkyl, phenyl optionally substituted with up to three substituents independently selected from the group consisting of halo and

5

10

15

20

 C_1 - C_4 alkoxy, pyridinyl, imidazolyl optionally substituted on a nitrogen atom with C_3 - C_6 cycloalkyl, morpholin-4-yl, pyrrolidin-1-yl, -CO₂H, -CO(C_1 - C_4 alkoxy), -CO(NR^8R^9), - NR^8R^9 or -(morpholin-4-yl)carbonyl;

 R^6 is hydrogen, C_1 - C_{10} alkyl optionally substituted with up to three halo substituents, 1-amino-2-methoxyeth-1-yl, C_3 - C_6 cycloalkyl, pyridinyl optionally substituted with C_1 - C_4 alkyl, trifluoromethyl, carboxyl, or $(C_1$ - C_4 alkoxy)carbonyl, pyridinyl-N-oxide, pyrazinyl, pyrimidinyl, imidazolyl, morpholin-4-yl optionally substituted with up to two C_1 - C_4 alkyl groups, [1,4]oxazepin-4-yl, azetidin-4-yl, tetrahydropyran-4-yl, 3-methyl-6,7-dihydropyrrolo[1,2-a]imidazol-6-yl, piperazin-4-yl optionally substituted in the 4-position with phenyl or C_1 - C_4 alkyl, pyrrolidin-1-yl, piperidin-1-yl optionally substituted in the 4-position with oxo or geminal dimethyl, piperidin-4-yl optionally substituted in the 1-position with $(C_1$ - C_4 alkoxy)carbonyl or C_1 - C_4 alkyl, or - $(C_1$ - C_4 alkylene)- R^{10} ;

 R^7 is C_1 - C_6 alkyl optionally substituted with halo, 2-methoxyeth-1-yl, -(C_1 - C_2 alkylene)-(morpholin-4-yl or pyrrolidin-2-on-1-yl), or phenyl optionally substituted with one or two substituents independently selected from the group consisting of halo, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, and trifluoromethyl;

R⁸ is hydrogen or C₁-C₆ alkyl optionally substituted with C₁-C₄ alkoxy;

R⁹ is hydrogen or C₁-C₆ alkyl optionally substituted with C₁-C₄ alkoxy;

R¹⁰ is -OCH₂CH₂OCH₃, -NR¹⁴R¹⁵, C₃-C₆ cycloalkyl, morpholin-4-yl,
thiomorpholin-4-yl, 1,1-dioxothiomorpholin-4-yl, piperidin-1-yl, pyrrolidin-2-yl
optionally substituted at the 1-position with C₁-C₄ alkyl, or imidazolyl optionally
substituted with nitro;

Ar is benzofur-4-yl, benzofur-7-yl, benzothien-4-yl, benzothien-7-yl, 1
(R¹¹)benzimidazol-4-yl, 1-(R¹¹)indol-4-yl, indol-7-yl, isoquinolin-5-yl, 2,3-dihydrobenzofur-4-yl, 2,3-dihydrobenzofur-7-yl, 1,3-dihydroisobenzofur-4-yl, 1,3-dihydroisobenzofur-5-yl, benzo[1,3]dioxol-4-yl, benzo[1,3]dioxol-5-yl, 2,3-dihydrobenzo[1,4]dioxin-5-yl, 2,3-dihydrobenzo[1,4]dioxin-6-yl, 2',2'-difluorobenzo[1,3]dioxol-4-yl, or 2',2'-difluorobenzo[1,3]dioxol-5-yl each optionally substituted in the phenyl ring with substituents R¹²

and R¹³, or Ar is a group selected from imidazo[1,2-a]pyridin-3-yl optionally substituted with one or two substituents independently selected from the group consisting of halo, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, benzyloxy, cyano, and trifluoromethyl, 5,6.7.8-

WO 03/076442 PCT/US03/05050

-155-

tetrahydroimidazo[1,2-a]pyridin-3-yl, imidazo[1,2-a]pyridin-5-yl, imidazo[1,2-a]pyrimidin-3-yl optionally substituted with amino, imidazo[1,2-a]pyrimidin-3-yl, imidazo[1,2-a]pyrazin-3-yl, imidazo[1,2-a]pyridazin-3-yl, imidazo[2,1-a]thiazol-3-yl, thiazolo[3,2-a][1,2,4]triazol-6-yl, furo[3,2-a]pyridin-7-yl optionally substituted with halo or -NR¹⁴R¹⁵, thieno[3,2-a]pyridin-7-yl, pyrazolo[1,5-a]pyridin-3-yl, or 4,5,6,7-tetrahydropyrazolo[1,5-a]pyridin-3-yl;

R¹¹ is hydrogen, C₁-C₄ alkyl, or -(CH₂)_P-G;

R¹² is halo, hydroxy, amino, C₁-C₄ alkoxy, -NHC(O)(C₁-C₄ alkyl), or

-O-(CH₂)_p-G;

5

30

 R^{13} is halo:

p is 2, 3, 4, or 5;

G is hydroxy or NR¹⁴R¹⁵;

 R^{14} and R^{15} are independently selected from the group consisting of hydrogen and C_1 - C_5 alkyl;

15 R¹⁶ is hydrogen or cyano,

 R^{17} is $-NR^8R^9$, C_1 - C_4 alkyl, morpholin-4-yl, or piperidin-1-yl; or a pharmaceutically acceptable salt thereof, provided that when n is 0, W-X-Y is not $-CH(R^{3'})-N(R^2)-C(O)$ -.

- 2. A compound of Claim 1 where Ar is benzofur-4-yl, benzofur-7-yl, or 2,3-dihydrobenzofur-7-yl optionally substituted in the phenyl ring with substituents R¹² and R¹³.
- A compound of Claim 1 where Ar is imidazo[1,2-a]pyridin-3-yl optionally
 substituted with one or two groups independently selected from halo, C₁-C₄ alkyl, or C₁-C₄ alkoxy.
 - 4. A compound of any of Claims 1, 2, or 3 where W-X-Y is -CH(R³)-N(R²)-CH(R³).
 - 5. A compound of Claim 4 where R^2 is $-C(O)R^6$.

- 6. A pharmaceutical formulation comprising a compound of any of Claims 1-5 in combination with a pharmaceutically acceptable carrier, diluent or excipient.
- 7. A method of treating diabetes in a mammal comprising administering to a
 5 mammal in need of such treatment an effective amount of a compound of any of Claims
 1-5.
- 8. A method of treating Alzheimer's disease in a mammal comprising administering to a mammal in need of such treatment an effective amount of any of Claims 1-5.
 - 9. A method of inhibiting GSK-3 in a mammal comprising administering to a mammal in need of such treatment a GSK-3 inhibiting amount of a compound of any of Claims 1-5.